IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Shinji OKANO et al.	Confirmation No.:	5137
Serial No.:	10/578,085	Art Unit:	1633
371 (c) Date:	May 3, 2006	Examiner:	Quang NGUYEN
Customer No.:	21559		
Title:	METHOD FOR PRODUCING GENE TRANSFERRED DENDRITIC CELLS		

REQUEST TO CORRECT FILING RECEIPT

Applicants request that the enclosed filing receipt be corrected as follows.

On page 2, under **Title**, please change "Denritic" to "Dendritic."

Enclosed are copies of the incorrect filing receipt and the Preliminary Amendment, as filed on May 3, 2006, which shows the correct information.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 11 January 2011

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APPLICATION NUMBER	FILING or 371(c) DATE	GRP ART UNIT	FIL FEE REC'D	ATTY DOCKET NO	TOT CLAIMS	IND CLAIMS
10/578,085	05/03/2006	1633	1440	50026/058001	14	2

CONFIRMATION NO. 5137

21559
CLARK & ELBING LLP
101 FEDERAL STREET
BOSTON, MA 02110

CORRECTED FILING RECEIPT

Date Mailed: 11/02/2007

Receipt is acknowledged of this non-provisional patent application. The application will be taken up for examination in due course. Applicant will be notified as to the results of the examination. Any correspondence concerning the application must include the following identification information: the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Filing Receipt Corrections. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections**

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Power of Attorney: The patent practitioners associated with Customer Number 21559

Domestic Priority data as claimed by applicant

This application is a 371 of PCT/JP04/16089 10/29/2004

Foreign Applications

JAPAN 2004-187028 06/24/2004
JAPAN 2003-374808 11/04/2003

If Required, Foreign Filing License Granted: 08/11/2007

The country code and number of your priority application, to be used for filing abroad under the Paris Convention, is **US 10/578,085**

Projected Publication Date: 11/22/2007

Non-Publication Request: No

Early Publication Request: No

Title

Method for Producing Gene Transferred ~~Denritic~~ Dendritic Cells

Preliminary Class

424

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Title 35, United States Code, Section 184

Title 37, Code of Federal Regulations, 5.11 & 5.15

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PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Shinji Okano et al.	Art Unit:	Not yet assigned
Serial No.:	Not yet assigned	Examiner:	Not yet assigned
Filed:	May 2, 2006	Customer No.:	21559
Title:	METHOD FOR PRODUCING GENE TRANSFERRED DENDRITIC CELLS (as amended)		

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PRELIMINARY AMENDMENT

Prior to examination of the above-captioned application, kindly amend the application as follows. Please note that all page and line number references in the present amendment refer to the concurrently filed English language translation of International Application No. PCT/JP2004/016089, of which the above-captioned application is the U.S. National Stage.

AMENDMENTS TO THE SPECIFICATION

Kindly amend the title of the application as follows.

METHOD ~~OF CONSTRUCTING TRANSGENIC~~ FOR PRODUCING GENE TRANSFERRED DENDRITIC ~~CELL~~ CELLS

Kindly insert the following heading and paragraph at page 1, line 4 of the English language specification.

Cross-Reference to Related Applications

This application is the U.S. National Stage of International Application No. PCT/JP2004/016089, filed October 29, 2004, which, in turn, claims the benefit of Japanese Patent Application Nos. 2004-187028, filed June 24, 2004, and 2003-374808, filed November 4, 2003.

Kindly amend the paragraph starting at page 10, line 16 of English language specification as follows.

In addition, the dendritic cells of the present invention include both mature and immature dendritic cells. The immature dendritic cells refer to dendritic cells having low T cell activating ability. Specifically, the immature dendritic cells may have an antigen-presenting ability that is lower than 1/2, preferably lower than 1/4 of that of dendritic cells which maturation had been induced by adding LPS (1 μg/ml) and culturing for two days.

The antigen-presenting ability can be assayed, for example, by allo T cell-activating ability (e.g., a mixed lymphocyte test: allo T cells and dendritic cells are cultured in a mixed culture with a T cell:dendritic cell ratio of 1:10, or preferably with varied ratios; ^{3}H-thymidine is added 8 hours before terminating cultivation, and the T cell growth capacity is assayed based on the amount of ^{3}H-thymidine incorporated into the DNA of the T cells. See Fig. 21; Gene Therapy 2000; 7; 249-254) or by the ability to induce specific cytotoxic T cells (CTLs) using a peptide (e.g., a known class I-restricted peptide of a certain antigen is added to dendritic cells; the dendritic cells are co-cultured with T cells obtained from peripheral blood of the same healthy donor from whom the dendritic cells had been obtained (with 25 U/ml or preferably 100 U/ml of IL-2 on day 3 or later) (preferably stimulated three times during 21 days, more preferably twice during 14 days by dendritic cells); the resulting effector cells are co-cultured with ^{51}Cr-labeled target cells (~~peptide~~ class I-restricted ~~class I~~ peptide positive tumor cells) at a ratio of 20:1, 10:1, 5:1, or 2.5:1, preferably 100:1, 50:1, 25:1, or 12.5:1, for four hours; and ^{51}Cr released from the target cells is quantified. See Fig. 22; Arch Dermatol Res 292:325-332 (2000)). Furthermore, the immature dendritic cells preferably have phagocytic ability for antigens, and more preferably show low (for example, significantly low as compared to mature DCs induced by LPS as described above) or negative expression of receptors that induce the costimulation for T cell activation. On the other hand, the mature dendritic cells refer to dendritic cells that have strong antigen-presenting ability for T cell activation or the

like. Specifically, the mature dendritic cells may have an antigen-presenting ability that is half or stronger, preferably equivalent to or stronger than the antigen-presenting ability of dendritic cells in which maturation has been induced by adding LPS (1 μg/ml) and culturing for two days. Furthermore, the mature dendritic cells preferably have weak or no phagocytic ability for antigen, and more preferably show high expression of receptors that induce the costimulation for T cell activation. The activation of dendritic cells refers to the transition from immature to mature dendritic cell; and the activated dendritic cells encompass mature dendritic cells and dendritic cells in the process of the transition, wherein the expression of CD80 and CD86 that induce costimulatory signals are elevated upon the activating stimuli. In CD11c positive dendritic cells, CD83 positivity serves as an indicator of mature dendritic cells.

Kindly amend the paragraph starting at page 12, line 26 of the English language specification as follows.

CD40 is a type I integral membrane protein of 45 to 48 kD (type I integral membrane glycoprotein). ~~Anti-CD40 antibody~~ CD40 is frequently used as a cell marker (Schlossman, S. *et al.*, eds., 1995, Leucocyte Typing V: White Cell Differentiation Antigens. Oxford University Press, New York; Galy, A.H.M.; and H. Spits, 1992, J. Immunol. 149: 775; Clark, E.A. and J.A. Ledbetter, 1986, Proc. Natl. Acad. Sci. 83:

4494; Itoh, H. *et al.*, 1991, Cell 66: 233; Barclay, N.A. *et al.*, 1993, The Leucocyte Antigen Facts Book., Academic Press).

Kindly amend the paragraph starting at page 17, line 31 of the English language specification as follows.

Herein, a minus-strand RNA virus refers to viruses that include a minus strand (an antisense strand corresponding to a sense strand encoding viral proteins) RNA as the genome. The minus-strand RNA is also referred to as negative strand RNA. The minus-strand RNA virus used in the present invention particularly includes single-stranded minus-strand RNA viruses (also referred to as non-segmented minus-strand RNA viruses). The "single-strand negative strand RNA virus" refers to viruses having a single-stranded negative strand [*i.e.*, a minus strand] RNA as the genome. The minus-strand RNA virus includes ~~Such viruses include~~ viruses belonging to Paramyxoviridae (including the genera *Paramyxovirus*, *Morbillivirus*, *Rubulavirus*, and *Pneumovirus*), Rhabdoviridae (including the genera *Vesiculovirus*, *Lyssavirus*, and *Ephemerovirus*), Filoviridae, Orthomyxoviridae, (including Influenza viruses A, B, and C, and Thogoto-like viruses), Bunyaviridae (including the genera *Bunyavirus*, *Hantavirus*, *Nairovirus*, and *Phlebovirus*), Arenaviridae, and the like.

Kindly amend the paragraph starting at page 33, line 26 of the English language specification as follows.

There is no limitation on the foreign gene to be introduced using the minus-strand RNA virus, and naturally occurring proteins include, for example, hormones, cytokines, growth factors, receptors, intracellular signaling molecules, enzymes, and peptides. The proteins may be secretory proteins, membrane proteins, cytoplasmic proteins, nuclear proteins, and the like. Artificial proteins include, for example, fusion proteins such as chimeric toxin, dominant negative proteins (including soluble receptor molecules or membrane bound dominant negative receptors), truncated cell adhesion molecules, and cell surface molecules. The proteins may also be proteins to which a secretory signal, membrane-localization signal, nuclear translocation signal, or the like has been attached. Functions of a particular gene can be suppressed by introducing and expressing antisense RNA molecule, RNA-cleaving ribozyme, or the like as the transfer gene. When a viral vector is prepared using a gene for treating diseases as the foreign gene, gene therapy can be performed through the introduction of the vector. The viral vector of the present invention is applicable to gene therapy wherein the genes are expressed by direct administration or by *ex vivo* administration, and enables expression of foreign genes for which therapeutic effect can be expected, internal genes short in *in vivo* supply, or the like from dendritic cells. In addition, the ~~method~~ vector of the present invention can also be used as a gene therapy vector in regeneration medicine.

Kindly amend the paragraph starting at page 35, line 36 of the English language specification as follows.

Antigens derived from pathogens include, for example, proteins of hepatitis A virus, hepatitis B virus, hepatitis C virus, hepatitis delta virus, papilloma virus antigen, herpes simplex virus (HSV), varicella-zoster virus (VZV), Epstein-Barr virus, Cytomegalovirus (CMV), HIV, malaria, and the like, or partial peptides thereof. The minus-strand RNA viruses encoding such antigen proteins can be used prophylactically or therapeutically. Specifically, envelopes of influenza highly-virulent strain H5N1 for influenza, envelope proteins of Japanese encephalitis virus (Vaccine, vol. 17, No. 15-16, 1869-1882 (1999)) for Japanese encephalitis, HIV and SIV gag proteins (J. Immunology (2000) vol. 164, 4968-4978), HIV envelope proteins, Nef protein, and other viral proteins for AIDS can be mentioned. In addition, for example, cholera toxin B subunit (CTB) (Arakawa T, *et al.*, Nature Biotechnology (1998) 16(10): 934-8, Arakawa T, *et al.*, Nature Biotechnology (1998) 16(3): 292-7) for cholera; rabies virus glycoprotein (Lodmell DL *et al.*, 1998, Nature Medicine 4(8):949-52) for rabies; and capsid protein L1 of human papilloma virus type 6 (J. Med. Virol, 60, 200-204 (2000)) for cervical carcinoma can be mentioned. Antigen proteins of other pathogenic viruses can also be expressed from the vector. Furthermore, it is possible to use JE-E antigen protein of Japanese encephalitis virus (Japanese Patent Application Kokai Publication No. (JP-A) S64-74982

(unexamined, published Japanese patent application), JP-A H1-285498), gD2 protein of human herpes simplex virus (JP-A H5-252965), polypeptides derived from hepatitis C virus (JP-A H5-192160), polypeptides derived from pseudorabies virus (Japanese Patent Kohyo Publication No. (JP-A) H7-502173 (unexamined Japanese national phase publication corresponding to a non-Japanese international publication), and the like. For example, cells derived from patients infected with such pathogenic microorganisms may be analyzed to identify an epitope of an antigen protein to be presented on antigen-presenting cells (APC) for use. It is preferred to appropriately select the HLA type and identify an epitope corresponding to the desired HLA for use.

REMARKS

The title has been amended and a paragraph cross-referencing related applications has been added. The paragraph starting at page 10, line 16 of English language specification has been amended to recite "class I-restricted peptide." Support for this change may be found, for example, at page 10, lines 26-27, and is further apparent from the context. The paragraph starting at page 12, line 26, has been amended to recite "CD40 is frequently used as a cell marker." Support for this change may be found, for example, at page 12, line 26, which recites "CD40." The paragraph starting at page 17, line 31 has been amended to recite "The minus-strand RNA virus includes." Support for this change may be found, for example, at page 17, line 31 which recites "a minus-strand RNA virus." Further support for this change may be found at page 18, lines 1-6, as the exemplified viruses are collectively known in the art as "minus strand RNA viruses." The paragraph starting at page 33, line 26 has been amended to recite "the vector of the present invention." Support for this change may be found, for example, at page 34, lines 1-2, which recite "The viral vector of the present invention." It is further apparent from the context that a vector, rather than a method, (page 34, lines 5-6; emphasis added) "can also be used as a gene therapy vector." Finally, the paragraph starting at page 35, line 36 has been amended to recite "Japanese encephalitis virus." Support for this change may be found at page 36, lines 5-6, which recites "Japanese encephalitis virus." Further, it is

apparent from the context that the JE-E antigen protein would be of Japanese encephalitis virus, rather than of Japanese encephalitis. These amendments add no new matter.

If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 3 May 2006

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